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The effect of anxiety on metabolic parameters in patients with primary hypertension

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ABSTRACT

Aims: Although the role of anxiety in the pathogenesis of hypertension is known, the effect of anxiety on metabolic parameters in hypertension has not been demonstrated. This study aimed to evaluate the effect of anxiety on metabolic parameters and blood pressure regulation in patients with primary hypertension.

Methods: The study was designed as a single-center, descriptive cross-sectional study. A total of 150 patients receiving antihypertensive therapy for primary hypertension were included in the study. Patients were divided into minimal, mild, moderate, and severe anxiety groups according to the Beck Anxiety Inventory. Anthropometric measurements, metabolic parameters, and blood pressure measurements were compared between groups.

Results: Significant positive correlations were found between anxiety severity and total cholesterol, LDL cholesterol, body mass index, and waist circumference ($p<0.05$). Subgroup analyses showed that total cholesterol, LDL cholesterol, body mass index, and waist circumference were higher in the severe anxiety group than in the minimal anxiety group ($p<0.05$).

Conclusion: Anxiety in patients with primary hypertension appears to have negative consequences on total cholesterol, LDL cholesterol, body mass index, and waist circumference. In hypertension, female gender and obesity are associated with increased anxiety levels.

Keywords: Hypertension, anxiety disorders, cholesterol, body mass index

INTRODUCTION

Cardiovascular diseases remain the most important cause of morbidity and mortality today.[1] Atherosclerotic disease, which is the basis of cardiovascular diseases, progresses insidiously, and combating risk factors is critical in preventing the development of cardiovascular disease.[1] Hypertension and dyslipidemia are the most important modifiable risk factors for cardiovascular disease.[2]

Findings in studies conducted in the United States population indicate that optimal total cholesterol levels are approximately 150 mg/dL (3.8 mmol/L), which corresponds to approximately 100 mg/dL (2.6 mmol/L) of low-density lipoprotein cholesterol (LDL-C). Adult populations with cholesterol concentrations in this range are accepted to be at low risk for atherosclerotic cardiovascular disease. Although LDL-C is the main causative parameter associated with atherosclerosis, other risk factors also contribute to the development of atherosclerosis, including smoking, hypertension, hyperglycemia, and other lipoprotein abnormalities.[3]

Metabolic syndrome is a complex condition that has risk factors interrelated with the development of cardiovascular diseases and diabetes. These factors include hyperglycemia, high blood pressure, high triglyceride levels, low high-density lipoprotein cholesterol (HDL-C) levels, and obesity (especially central adiposity).[4]

Anxiety disorders are associated with the onset and progression of heart disease and in many cases, are also related to adverse cardiovascular outcomes, including mortality. Both behavioral and physiological mechanisms (autonomic dysfunction, inflammation, endothelial dysfunction, changes in platelet aggregation) may help explain the associations between anxiety and cardiovascular disease. Individuals with anxiety tend to increase dietary cholesterol intake and total energy intake, adopt a sedentary lifestyle, and reduce physical activity. These are consistent with findings showing that patients with anxiety have increased rates of dyslipidemia, obesity, diabetes, and substance use.[5]

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The present study aimed to reveal the effects of anxiety on metabolic parameters and blood pressure control in patients with primary hypertension under treatment.

METHODS

Between May 2018 and September 2018, 150 patients with primary hypertension who were receiving antihypertensive therapy were included in the study. Patients under 18 years of age, with secondary hypertension, diabetes mellitus (DM), chronic kidney disease (glomerular filtration rate (GFR) <60 mL/min/1.73 m^2), hyperlipidemia, coronary artery disease, smoking and alcohol use, hyperthyroidism or hypothyroidism, pregnancy, psychiatric disease, Alzheimer's disease, and those using any psychiatric drugs (antidepressant, anxiolytic, antipsychotic, etc.) or antihyperlipidemic drugs were excluded from the study. Written informed consent was obtained from all patients. The Clinical Researches Ethics Committee of the institution approved the study protocol (Date: 09.05.2018 Decision No: 2018/7-09). The study was carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The Beck Anxiety Inventory (BAI) for assessment of the severity of anxiety was applied to all patients. The BAI is a 21-item scale used to determine the severity of anxiety. Participants are asked the level of discomfort they have felt regarding each of the items (symptoms) within the past week. The degree of discomfort is scored between 0 (never) and 3 (severe – hardly bearable). The total score ranges between 0 and 63. The BAI scores classification was defined as follows: 0-7 minimal anxiety symptoms, 8-15 mild anxiety symptoms, 16-25 moderate anxiety symptoms, and 26-63 severe anxiety symptoms. The patients were divided into the respective groups (minimal, mild, moderate, and severe anxiety) according to the scores obtained from the BAI. Patients were asked to do a one-week home blood pressure monitoring under their current antihypertensive treatment.

In the morning after 12 hours of fasting, blood was taken from the patients, and fasting plasma glucose and lipid parameters (total cholesterol, LDL-C, HDL-C, triglyceride) were measured on the same day. Fasting plasma glucose and lipid parameters were measured using a Beckman Coulter AU680 device (Beckman Coulter, Miami, FL, USA) with original reagents. LDL-C level was calculated with the Friedewald formula [LDL-C = Total cholesterol – HDL-C – (Triglyceride/5)] in patients with triglyceride levels of <400 mg/dL, while LDL-C was directly measured in patients with triglyceride levels higher than 400 mg/dL. The GFR was calculated with the Modification of Diet in Renal Disease (MDRD) GFR equation [Estimated GFR (mL/min/1.73 m^2) = 186 × (Serum creatinine$^{-1.154}$) × (age$^{-0.203}$) × 0.742 (if female)]. Patients with estimated GFR <60 mL/min/1.73 m^2 were not included in the study.

Anthropometric measurements including weight, height, and waist circumference were obtained. The height of the patients was measured by portable stadiometers. Body weight was measured by trained healthcare professionals with participants standing without shoes in light indoor clothing, using a digital scale. Waist circumference was measured midway between the lowest border of the rib cage and the upper border of the iliac crest, at the end of normal expiration. Body mass index (BMI) was calculated as the ratio of body weight in kilograms to the square of height in meters. A BMI over 30 kg/m^2 is considered obese.

Statistical Analysis

It was performed using SPSS version 22.0 for Windows statistical software (IBM SPSS Statistics, Chicago, IL, USA). The data were expressed as mean±standard deviation for continuous variables and as proportions for categorical variables. The normal distributions of continuous variables were evaluated with the Shapiro-Wilk test. The One-way ANOVA test was used to compare normally distributed variables. The Kruskal-Wallis test was used for the comparison of non-normally distributed variables. Correlation analyses were performed using Pearson's correlation analysis for normally distributed variables, and Spearman's correlation analysis for non-normally distributed variables. Categorical parameters were analyzed using the Chi-square test. For all analyses, $p<0.05$ was considered statistically significant.

RESULTS

Of the 150 patients included in the study, 125 (83.3%) were women. The average age of the patients was 55±10 years, and the age range was 27-73 years. According to the BAI scores, 37 patients (22 women, 15 men) had minimal anxiety symptoms, 41 patients (33 women, 8 men) had mild anxiety symptoms, 45 patients (43 women, 2 men) had moderate anxiety symptoms, and 27 patients (all women) had severe anxiety symptoms.

The anthropometric and clinical characteristics of the patients according to the anxiety symptom groups are shown in Table 1. It was observed that as the anxiety severity of the groups increased, the female gender ratio also increased. BAI score was higher in female hypertensive patients than in males (18.5±11.6 vs 6.4±5.2, respectively, $p<0.001$). Significant differences were found in terms of gender, height, BMI, and waist circumference ($p<0.05$). In the subgroup analyses, BMI and waist circumference were found to be significantly higher, and height was found to be significantly lower in the severe anxiety group than in the minimal anxiety group ($p<0.05$). It was also observed that as the anxiety severity of

Table 1. Anthropometric and clinical characteristics of patients by anxiety groups

	Minimal (n=37)	Mild (n=41)	Moderate (n=45)	Severe (n=27)	p-value
Age (years)	55.2±10.9	55.4±8.9	53.7±10.7	55.5±9.7	0.867
Female gender (n, %)	22 (59.5)	33 (80.5)	43 (95.6)	27 (100)	<0.001
Weight (kg)	79.8±14.8	80±13.3	79.8±5.1	83.4±14.2	0.937
Height (cm)	162.5±9.2	157.7±8.1	157.8±6.4	154.3±6.3	0.002
Body mass index (kg/m^2)	30.27±5.62	32.16±5.02	32.07±5.1	35.08±6.07	0.013
Obesity (n, %)	16 (43.2)	25 (61%)	34 (75.6)	22 (81.5)	0.004
Waist circumference (cm)	97±11	100±12	101±11	106±11	0.039
Hypertension duration (years)	6.3±4.9	7.1±5.8	7.3±7.5	9.9±7.1	0.245
Regularity of antihypertensive medication use (n, %)					
Regular	32 (86.5)	39 (95.1)	39 (86.7)	25 (92.6)	0.483
Irregular	5 (13.5)	2 (4.9)	6 (13.3)	2 (7.4)	
Number of antihypertensive medications (n, %)					
Monotherapy	9 (24.3)	9 (22)	9 (20)	11 (40.7)	0.622
Dual combination therapy	22 (59.5)	25 (61)	28 (62.2)	13 (48.2)	
Triple or greater combination therapy	6 (16.2)	7 (17)	8 (17.8)	3 (11.1)	

Data are given as mean ± standard deviation or number with percentage

Table 2. Blood pressure and antihypertensive medications of patients by anxiety groups

	Minimal (n=37)	Mild (n=41)	Moderate (n=45)	Severe (n=27)	p-value
Systolic blood pressure (mmHg)	124.3±12.2	124±11.4	125.5±10.8	128.8±11.6	0.339
Diastolic blood pressure (mmHg)	77.5±8.9	77.8±8.9	76.9±8.6	80.5±7.1	0.366
Controlled hypertension (n, %)	19 (51.4)	27 (65.9)	24 (53.3)	13 (48.1)	0.438
Antihypertensive medication (n, %)					
Angiotensin-converting enzyme inhibitors	6 (16.2)	9 (22.0)	9 (20.0)	9 (33.3)	0.416
Angiotensin receptor blockers	24 (64.9)	25 (61.0)	30 (66.7)	12 (44.4)	0.269
Calcium channel blockers	15 (40.5)	14 (34.1)	18 (40.0)	9 (33.3)	0.882
Beta-blockers	6 (16.2)	7 (17.1)	7 (15.6)	5 (18.5)	0.990
Diuretics	21 (56.8)	24 (58.5)	28 (62.2)	11 (40.7)	0.337

Data are given as mean ± standard deviation or number with percentage

the groups increased, the obesity ratio also increased. Obese hypertensive patients had higher BAI scores than non-obese patients (18.9±11.9 vs 12.1±10.1, respectively, p<0.001). There was no significant difference between the groups in terms of the duration of hypertension (p=0.245). Additionally, the regularity of antihypertensive medication use was found to be similar in the groups (p=0.483) and the frequency of regular medication use was over 86% in all groups.

The antihypertensive treatments of the patients were evaluated under three main groups; monotherapy, double combination therapy, and triple (or greater) combination therapy. Of the 150 patients, 38 (25.3%) were using antihypertensive monotherapy, 88 (58.7%) were using a double combination, and 24 (16%) were using triple or greater combination treatments. There was no difference between the anxiety groups in terms of the number of antihypertensive medications used (p=0.622).

Blood pressure and antihypertensive medications of patients according to the anxiety groups are shown in Table 2. When the systolic and diastolic pressures were examined, no significant differences were found between the groups. The most frequently used antihypertensive drug groups by the patients were angiotensin receptor blockers (60.7%), diuretics (56%), calcium channel blockers (37.3%), angiotensin-converting enzyme inhibitors (22%), and beta-blockers (16.7%), respectively. There was no difference between the groups in terms of antihypertensive medication groups.

The laboratory values of the patients according to the anxiety groups are shown in Table 3. There was a significant difference between the groups in terms of total cholesterol (p=0.029) and LDL-C (p=0.025). Subgroup analyses revealed that total cholesterol and LDL-C levels were significantly higher in the severe anxiety group than in the minimal anxiety group (p=0.007).

In the analysis of the study population, significant relationships were found between BAI score and total cholesterol, LDL-C, BMI, and waist circumference (Figure a, b, c, d).

Table 3. Laboratory values of patients by groups

	Minimal (n=37)	Mild (n=41)	Moderate (n=45)	Severe (n=27)	p-value
eGFR (ml/min/1.73 m^2)	81.4±14.6	80.4±12.9	79.3±13.7	80.7±15.5	0.909
Fasting plasma glucose (mg/dl)	99.2±11.5	99.9±11.7	98.5±11.5	96.3±8.7	0.616
Total cholesterol (mg/dl)	183.3±33.5	191.7±31.3	193.7±39.3	209.7±31.6	0.029
HDL-C (mg/dl)	47.5±13.7	48.1±10.8	48.2±8.9	49.3±10.6	0.934
LDL-C (mg/dl)	109.9±25.7	117.9±27.2	117.5±34.5	132.8±28.4	0.025
Triglyceride (mg/dl)	132.6±68.9	135.5±70.9	142±61	129.9±50.3	0.863

Data are given as mean ± standard deviation
Abbreviations: eGFR: Estimated glomerular filtration rate, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol

DISCUSSION

Hypertension and dyslipidemia are the most important modifiable risk factors for cardiovascular diseases. Anxiety disorder is the most common psychiatric disorder with a 12-month prevalence of 18.1%.[6] While there are many studies on hypertension and anxiety disorders separately, the number of studies investigating the relationship between these two diseases is relatively few. We found that BMI, waist circumference, total cholesterol, and LDL-C levels of patients with severe anxiety were found to be significantly higher compared to those with minimal anxiety symptoms. No significant difference was found between the other groups.

In the present study, 83.3% of the patients were women and the proportion of women was higher than that of men. In epidemiological studies, it has been shown that generalized anxiety disorder and panic disorder are approximately twice as common in women than in men.[7] In our study, as the anxiety severity of the groups increased, the women's frequency increased.

In our study, the BMI of the severe anxiety group was found to be significantly higher than the minimal anxiety group. Again, when the patients were compared in terms of obesity presence, we found that obesity was significantly more common in the severe anxiety group and the moderate anxiety group compared to the minimal anxiety group. These results are in line with the results of studies that report high obesity frequency in subjects with anxiety disorders.[8,9] In the study by Black et al.[10], it was shown that mood disorders, personality disorders, and anxiety disorders are higher in patients defined to be morbidly obese compared to their non-obese counterparts. As a result of not being able to cope with anxiety adequately, loss of control over eating occurs in those with anxiety disorders, and they have a tendency to eat more, and thus, become obese.[8]

In our study, no significant relationships were found between anxiety severity and systolic or diastolic blood pressure. In conclusion, no relationship was found between the level of anxiety and the regulation of hypertension under treatment. In a study that examined whether there was a relationship between anxiety disorders and resistant hypertension, although no direct relationship could be found between panic disorder and resistant hypertension, the prevalence of panic disorder was found to be quite high in hypertension patients.[11] The results of our study were similar to this study in terms of the lack of a relationship between the regulation

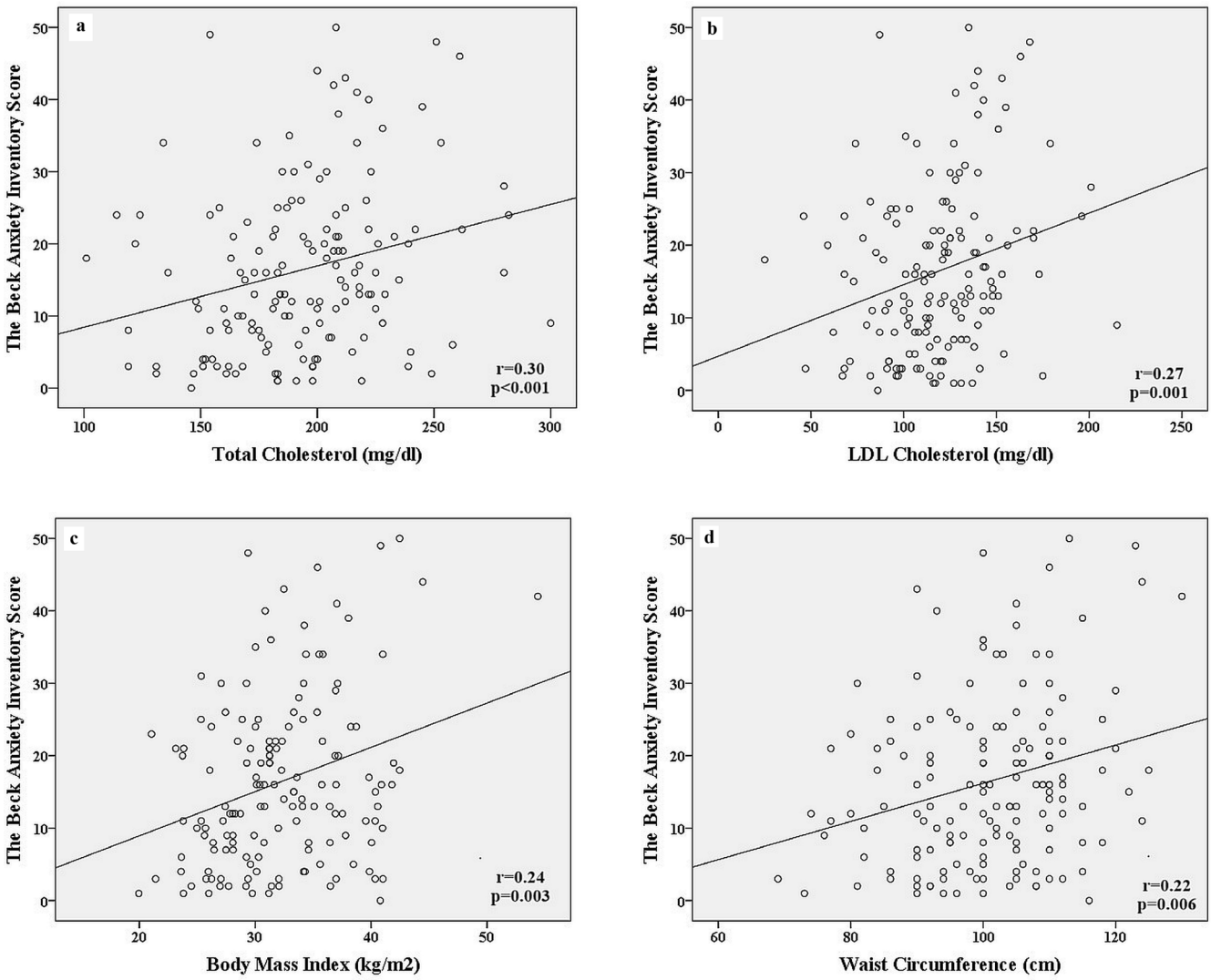

Figure. Relationships between The Beck Anxiety Inventory score and total cholesterol (**a**), low-density lipoprotein cholesterol (**b**), body mass index (**c**), and waist circumference (**d**).

of hypertension and the severity of anxiety. However, the conclusion in Kaplan's study that panic symptoms complicate the treatment of hypertension should also be kept in mind.[12] Symptoms frequently described by these patients are palpitations, dizziness, paresthesia, and headache. It should be noted that situations such as failure to detect panic symptoms by patients and physicians or linking symptoms to antihypertensive treatment may lead to inappropriate discontinuation and modification of antihypertensive treatments. In another study, the prevalence of hypertension in patients with panic disorder was found to be higher than in the normal population.[13] In another study, the prevalence of panic disorder in hypertension patients was found to have an approximately threefold increase.[14] To summarize, although anxiety disorders are a risk factor for hypertension, there is no direct relationship between these conditions in terms of resistance to treatment. More comprehensive studies are needed on this subject. It should be kept in mind that anxiety disorders and hypertension are two intertwined diseases.

In our study, the total cholesterol and LDL-C values have shown positive correlations with the severity of anxiety. In terms of other metabolic parameters (fasting plasma glucose, HDL-C, triglyceride), there was no relationship between the severity of anxiety and these parameters. The results of studies on this subject are quite different from each other. Many previous studies have shown that natural or induced stress and anxiety disorders may cause an increase in cholesterol levels.[15-19] In our study, the LDL-C and total cholesterol levels were found to be significantly higher in patients with severe anxiety compared to those with minimal anxiety, which supports previous studies. From this, it can be concluded that stress leads to an increase in cholesterol levels. It may be erroneous to try and treat high cholesterol levels by ignoring anxiety in patients with untreated anxiety. It is a well-established fact that stress increases the risk of cardiovascular events.[16] As shown in our study, anxiety can cause an increase in cholesterol levels, which may lead to an increase in cardiovascular risk. Although most of the relevant studies focused on panic disorder, a study examining generalized anxiety disorder also found a relationship with elevated cholesterol levels.[19] Based on these findings, it can be concluded that stress and anxiety disorders may increase cholesterol levels.

Generalized anxiety disorder often begins at an early age, has a chronic course, and is often associated with other mood disorders, as well as being comorbid with other diagnoses.[20] Those who used any psychiatric medication were not included in our study. It has been shown that many psychiatric drug groups (antipsychotics, antidepressants, anxiolytics, etc.) have positive or (mostly) negative effects on

metabolic parameters.[21-23] For example, many antipsychotic drugs can cause hyperglycemia, dyslipidemia, insulin resistance, and metabolic syndrome.[21] Although the exact mechanism has not been clarified, it is believed that various mechanisms may contribute to this outcome, including the inhibition of glucose uptake receptors in peripheral tissue, increased insulin secretion, and increased catecholamine levels.[21-24] Again, the central effect of antipsychotics and the increase in food intake are thought to be important factors in the development of these results.[21,25] It has been reported that selective serotonin reuptake inhibitors, which are frequently used in the treatment of anxiety, may also have positive or negative effects on metabolic parameters in a few studies, although the findings are different.[22,26] In light of this information, we excluded all parameters other than anxiety severity that could influence metabolic parameters positively or negatively, such as additional variables or drug use, to ensure the integrity of our data and to increase the accuracy of our findings.

Although there are many studies on hypertension, anxiety disorder, and hyperlipidemia, our literature review did not yield any studies examining these three issues in concert. Examining these three issues together can be considered as one of the strong aspects of our study. The most important limitation of the present study is the significantly high frequency of women in the study group.

CONCLUSION

Anxiety levels are higher in female hypertensive patients than in males. Anxiety levels are also higher in obese patients with hypertension than non-obese. The BMI, waist circumference, total cholesterol, and LDL-C levels are related to the severity of anxiety symptoms in patients with primary hypertension. Total cholesterol and LDL-C levels are increased in patients with severe anxiety. Severe anxiety in hypertension patients may increase the risk of cardiovascular disease by causing an increase in BMI, waist circumference, total cholesterol, and LDL-C levels. There is no relationship between the severity of anxiety and the regulation of blood pressure in hypertension patients receiving antihypertensive treatment. There is a need for more comprehensive studies exploring the effects of anxiety disorders on the increased risk of cardiovascular disease in patients with hypertension.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was initiated with the approval of the Kütahya Dumlupınar University Medical Faculty Clinical Researches Ethics Committee (Date: 09.05.2018, Decision No: 2018/7-09).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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